



# SEQUENCE LISTING

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Tian, Hui  
Zhong, Wendy Wen  
Tularik Inc.

<120> Receptor Ligands and Methods of Modulating Receptors

<130> 018781-009530US

<140> US 10/719,692

<141> 2003-11-21

<150> US 60/421,142

<151> 2002-11-25

<150> US 60/444,153

<151> 2003-01-30

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<170> PatentIn Ver. 2.1

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<212> DNA

<213> Homo sapiens

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gctccagagg cgtaaatggc caactccggt gagccatgga gccctcttta tctgggcccc 1080
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<212> PRT

<213> Homo sapiens

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<223> human G-protein coupled receptor TGR4a (HM74)

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			20					25					30			
Val	Leu	Gly	Leu	Glu	Phe	Ile	Phe	Gly	Leu	Leu	Gly	Asn	Gly	Leu	Ala	
		35					40					45				
Leu	Trp	Ile	Phe	Cys	Phe	His	Leu	Lys	Ser	Trp	Lys	Ser	Ser	Arg	Ile	
	50					55					60					
Phe	Leu	Phe	Asn	Leu	Ala	Val	Ala	Asp	Phe	Leu	Leu	Ile	Ile	Cys	Leu	
65					70					75					80	
Pro	Phe	Val	Met	Asp	Tyr	Tyr	Val	Arg	Arg	Ser	Asp	Trp	Asn	Phe	Gly	
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Gly	Ser	Ile	Ile	Phe	Leu	Thr	Val	Val	Ala	Val	Asp	Arg	Tyr	Phe	Arg	
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Val	Val	His	Pro	His	His	Ala	Leu	Asn	Lys	Ile	Ser	Asn	Trp	Thr	Ala	
	130					135					140					
Ala	Ile	Ile	Ser	Cys	Leu	Leu	Trp	Gly	Ile	Thr	Val	Gly	Leu	Thr	Val	
145					150					155					160	
His	Leu	Leu	Lys	Lys	Lys	Leu	Leu	Ile	Gln	Asn	Gly	Pro	Ala	Asn	Val	
			165					170						175		
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		180						185					190			
Phe	Leu	Leu	Glu	Phe	Leu	Leu	Pro	Leu	Gly	Ile	Ile	Leu	Phe	Cys	Ser	
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	210					215					220					
Lys	Ile	Lys	Arg	Ala	Ile	Thr	Phe	Ile	Met	Val	Val	Ala	Ile	Val	Phe	
225					230					235					240	
Val	Ile	Cys	Phe	Leu	Pro	Ser	Val	Val	Val	Arg	Ile	Arg	Ile	Phe	Trp	
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Leu	Leu	His	Thr	Ser	Gly	Thr	Gln	Asn	Cys	Glu	Val	Tyr	Arg	Ser	Val	
			260					265					270			
Asp	Leu	Ala	Phe	Phe	Ile	Thr	Leu	Ser	Phe	Thr	Tyr	Met	Asn	Ser	Met	
	275						280					285				
Leu	Asp	Pro	Val	Val	Tyr	Tyr	Phe	Ser	Ser	Pro	Ser	Phe	Pro	Asn	Phe	
	290					295					300					

Phe Ser Thr Leu Ile Asn Arg Cys Leu Gln Arg Lys Met Thr Gly Glu  
 305 310 315 320  
 Pro Asp Asn Asn Arg Ser Thr Ser Val Glu Leu Thr Gly Asp Pro Asn  
 325 330 335  
 Lys Thr Arg Gly Ala Pro Glu Ala Leu Met Ala Asn Ser Gly Glu Pro  
 340 345 350  
 Trp Ser Pro Ser Tyr Leu Gly Pro Thr Ser Asn Asn His Ser Lys Lys  
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 370 375 380  
 Cys Ile Glu  
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 <212> DNA  
 <213> Homo sapiens  
 <220>  
 <223> human G-protein coupled receptor TGR4b

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 gggcttcttg gcaatggcct tgccctgtgg attttctgtt tccacctcaa gtcttgga 180  
 tccagccgga ttttctgtt caacctggca gtggctgact ttctactgat catctgcttg 240  
 cccttctga tggacaacta tgtgaggcgt tgggactgga agtttgggga catcccttgc 300  
 cggctgatgc tcttcatgtt ggctatgaac cgccagggca gcatcatctt cctcacggtg 360  
 gtggcggtag acaggtattt ccgggtgggtc catccccacc acgccctgaa caagatctcc 420  
 aatcggacag cagccatcat ctcttgccct ctgtggggca tcaactattgg cctgacagtc 480  
 cacctcctga agaagaagat gccgatccag aatggcggtg caaatttgtg cagcagcttc 540  
 agcatctgcc ataccttcca gtggcacgaa gccatgttcc tcttgaggtt cttcctgccc 600  
 ctgggcatca tctgttctg ctcagccaga attatctgga gcctgcggca gagacaaatg 660  
 gaccggcatg ccaagatcaa gagagccatc accttcatca tgggtgggtggc catcgtcttt 720  
 gtcactctgt tcttcccag cgtggttgtg cggatccgca tcttctgggt cctgcacact 780  
 tcgggcacgc agaattgtga agtgtaccgc tcggtggacc tggcggttctt tatcactctc 840  
 agcttcacct acatgaacag catgctggac ccggtgggtg actacttctc cagcccatcc 900  
 tttcccaact tcttctccac tttgatcaac cgctgcctcc agaggaagat gacaggtgag 960  
 ccagataata accgcagcac gagcgtcgag ctcacagggg accccaacaa aaccagaggc 1020  
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 <213> Homo sapiens  
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 <223> human G-protein coupled receptor TGR4b

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			20					25					30				
Val	Leu	Gly	Leu	Glu	Phe	Ile	Phe	Gly	Leu	Leu	Gly	Asn	Gly	Leu	Ala		
		35					40					45					
Leu	Trp	Ile	Phe	Cys	Phe	His	Leu	Lys	Ser	Trp	Lys	Ser	Ser	Arg	Ile		
	50					55					60						
Phe	Leu	Phe	Asn	Leu	Ala	Val	Ala	Asp	Phe	Leu	Leu	Ile	Ile	Cys	Leu		
65					70					75					80		
Pro	Phe	Leu	Met	Asp	Asn	Tyr	Val	Arg	Arg	Trp	Asp	Trp	Lys	Phe	Gly		
				85					90					95			
Asp	Ile	Pro	Cys	Arg	Leu	Met	Leu	Phe	Met	Leu	Ala	Met	Asn	Arg	Gln		
			100					105					110				
Gly	Ser	Ile	Ile	Phe	Leu	Thr	Val	Val	Ala	Val	Asp	Arg	Tyr	Phe	Arg		
	115						120					125					
Val	Val	His	Pro	His	His	Ala	Leu	Asn	Lys	Ile	Ser	Asn	Arg	Thr	Ala		
	130					135					140						
Ala	Ile	Ile	Ser	Cys	Leu	Leu	Trp	Gly	Ile	Thr	Ile	Gly	Leu	Thr	Val		
145					150					155					160		
His	Leu	Leu	Lys	Lys	Lys	Met	Pro	Ile	Gln	Asn	Gly	Gly	Ala	Asn	Leu		
				165					170					175			
Cys	Ser	Ser	Phe	Ser	Ile	Cys	His	Thr	Phe	Gln	Trp	His	Glu	Ala	Met		
			180					185					190				
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	195						200					205					
Ala	Arg	Ile	Ile	Trp	Ser	Leu	Arg	Gln	Arg	Gln	Met	Asp	Arg	His	Ala		
	210					215					220						
Lys	Ile	Lys	Arg	Ala	Ile	Thr	Phe	Ile	Met	Val	Val	Ala	Ile	Val	Phe		
225					230					235					240		
Val	Ile	Cys	Phe	Leu	Pro	Ser	Val	Val	Val	Arg	Ile	Arg	Ile	Phe	Trp		
			245					250						255			
Leu	Leu	His	Thr	Ser	Gly	Thr	Gln	Asn	Cys	Glu	Val	Tyr	Arg	Ser	Val		
		260					265						270				
Asp	Leu	Ala	Phe	Phe	Ile	Thr	Leu	Ser	Phe	Thr	Tyr	Met	Asn	Ser	Met		
	275						280					285					
Leu	Asp	Pro	Val	Val	Tyr	Tyr	Phe	Ser	Ser	Pro	Ser	Phe	Pro	Asn	Phe		
	290					295					300						
Phe	Ser	Thr	Leu	Ile	Asn	Arg	Cys	Leu	Gln	Arg	Lys	Met	Thr	Gly	Glu		
305					310				315						320		
Pro	Asp	Asn	Asn	Arg	Ser	Thr	Ser	Val	Glu	Leu	Thr	Gly	Asp	Pro	Asn		
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 355 360

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 <212> DNA  
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 tgcttccaca tgaagacctg gaagcccagc actgtttacc ttttcaattt ggccgtggct 180  
 gatttcctcc ttatgatctg cctgcctttt cggacagact attacctcag acgtagacac 240  
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 caccacgcgg tgaacactat ctccaccggg gtggcggtg gcacgtctg caccctgtgg 420  
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 cagccaggac actcaaaaac acaaaggccg gaagagatgc caatttcgaa cctcgggtcg 960  
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 Asn Gly Val Ala Leu Cys Gly Phe Cys Phe His Met Lys Thr Trp Lys  
 35 40 45  
 Pro Ser Thr Val Tyr Leu Phe Asn Leu Ala Val Ala Asp Phe Leu Leu  
 50 55 60  
 Met Ile Cys Leu Pro Phe Arg Thr Asp Tyr Tyr Leu Arg Arg Arg His  
 65 70 75 80

Trp Ala Phe Gly Asp Ile Pro Cys Arg Val Gly Leu Phe Thr Leu Ala  
                             85                            90                            95  
 Met Asn Arg Ala Gly Ser Ile Val Phe Leu Thr Val Val Ala Ala Asp  
                             100                            105                            110  
 Arg Tyr Phe Lys Val Val His Pro His His Ala Val Asn Thr Ile Ser  
                             115                            120                            125  
 Thr Arg Val Ala Ala Gly Ile Val Cys Thr Leu Trp Ala Leu Val Ile  
                             130                            135                            140  
 Leu Gly Thr Val Tyr Leu Leu Leu Glu Asn His Leu Cys Val Gln Glu  
                             145                            150                            155                            160  
 Thr Ala Val Ser Cys Glu Ser Phe Ile Met Glu Ser Ala Asn Gly Trp  
                             165                            170                            175  
 His Asp Ile Met Phe Gln Leu Glu Phe Phe Met Pro Leu Gly Ile Ile  
                             180                            185                            190  
 Leu Phe Cys Ser Phe Lys Ile Val Trp Ser Leu Arg Arg Arg Gln Gln  
                             195                            200                            205  
 Leu Ala Arg Gln Ala Arg Met Lys Lys Ala Thr Arg Phe Ile Met Val  
                             210                            215                            220  
 Val Ala Ile Val Phe Ile Thr Cys Tyr Leu Pro Ser Val Ser Ala Arg  
                             225                            230                            235                            240  
 Leu Tyr Phe Leu Trp Thr Val Pro Ser Ser Ala Cys Asp Pro Ser Val  
                             245                            250                            255  
 His Gly Ala Leu His Ile Thr Leu Ser Phe Thr Tyr Met Asn Ser Met  
                             260                            265                            270  
 Leu Asp Pro Leu Val Tyr Tyr Phe Ser Ser Pro Ser Phe Pro Lys Phe  
                             275                            280                            285  
 Tyr Asn Lys Leu Lys Ile Cys Ser Leu Lys Pro Lys Gln Pro Gly His  
                             290                            295                            300  
 Ser Lys Thr Gln Arg Pro Glu Glu Met Pro Ile Ser Asn Leu Gly Arg  
                             305                            310                            315                            320  
 Arg Ser Cys Ile Ser Val Ala Asn Ser Phe Gln Ser Gln Ser Asp Gly  
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<212> DNA

<213> Homo sapiens

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<223> human G-protein coupled receptor TGR4a allele 2

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tccagccgga ttttcctgtt caacctggca gtagctgact ttctactgat catctgcctg 240
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cggctggtgc tcttcatgtt tgccatgaac cgccagggca gcatcatctt cctcacgggtg 360
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aattggacag cagccatcat ctcttgccct ctgtggggca tcaactgttg cctaacagtc 480
cacctcctga agaagaagtt gctgatccag aatggccctg caaatgtgtg catcagcttc 540
agcatctgcc ataccttccg gtggcacgaa gctatgttcc tcttgaggtt cctcctgccc 600
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gctccagagg cgtaaattggc caactccggt gagccatgga gcccctctta tctgggccc 1080
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<213> Homo sapiens

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<223> human G-protein coupled receptor TGR4a allele 2

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Val Leu Gly Leu Glu Phe Ile Phe Gly Leu Leu Gly Asn Gly Leu Ala
      35             40             45

Leu Trp Ile Phe Cys Phe His Leu Lys Ser Trp Lys Ser Ser Arg Ile
      50             55             60

Phe Leu Phe Asn Leu Ala Val Ala Asp Phe Leu Leu Ile Ile Cys Leu
      65             70             75             80

Pro Phe Val Met Asp Tyr Tyr Val Arg Arg Ser Asp Trp Lys Phe Gly
      85             90             95

Asp Ile Pro Cys Arg Leu Val Leu Phe Met Phe Ala Met Asn Arg Gln
      100            105            110

Gly Ser Ile Ile Phe Leu Thr Val Val Ala Val Asp Arg Tyr Phe Arg
      115            120            125

Val Val His Pro His His Ala Leu Asn Lys Ile Ser Asn Trp Thr Ala
      130            135            140

Ala Ile Ile Ser Cys Leu Leu Trp Gly Ile Thr Val Gly Leu Thr Val
      145            150            155            160

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His Leu Leu Lys Lys Lys Leu Leu Ile Gln Asn Gly Pro Ala Asn Val  
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 180 185 190  
 Phe Leu Leu Glu Phe Leu Leu Pro Leu Gly Ile Ile Leu Phe Cys Ser  
 195 200 205  
 Ala Arg Ile Ile Trp Ser Leu Arg Gln Arg Gln Met Asp Arg His Ala  
 210 215 220  
 Lys Ile Lys Arg Ala Ile Thr Phe Ile Met Val Val Ala Ile Val Phe  
 225 230 235 240  
 Val Ile Cys Phe Leu Pro Ser Val Val Val Arg Ile Arg Ile Phe Trp  
 245 250 255  
 Leu Leu His Thr Ser Gly Thr Gln Asn Cys Glu Val Tyr Arg Ser Val  
 260 265 270  
 Asp Leu Ala Phe Phe Ile Thr Leu Ser Phe Thr Tyr Met Asn Ser Met  
 275 280 285  
 Leu Asp Pro Val Val Tyr Tyr Phe Ser Ser Pro Ser Phe Pro Asn Phe  
 290 295 300  
 Phe Ser Thr Leu Ile Asn Arg Cys Leu Gln Arg Lys Met Thr Gly Glu  
 305 310 315 320  
 Pro Asp Asn Asn Arg Ser Thr Ser Val Glu Leu Thr Gly Asp Pro Asn  
 325 330 335  
 Lys Thr Arg Gly Ala Pro Glu Ala Leu Met Ala Asn Ser Gly Glu Pro  
 340 345 350  
 Trp Ser Pro Ser Tyr Leu Gly Pro Thr Ser Asn Asn His Ser Lys Lys  
 355 360 365  
 Gly His Cys His Gln Glu Pro Ala Ser Leu Glu Lys Gln Leu Gly Cys  
 370 375 380  
 Cys Ile Glu  
 385

<210> 9

<211> 200

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:poly-Gly  
flexible linker

<220>

<221> MOD\_RES

<222> (6)..(200)

<223> Gly residues from position 6 to 200 may be present  
or absent



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 20 25 30  
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly  
 35 40 45  
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly  
 50 55 60  
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly  
 65 70 75 80  
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly  
 85 90 95  
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly  
 100 105 110  
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly  
 115 120 125  
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly  
 130 135 140  
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly  
 145 150 155 160  
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 165 170 175  
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly  
 180 185 190  
 Gly Gly Gly Gly Gly Gly Gly Gly  
 195 200